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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,873	11/01/2002	Anand Ranganathan	SHW-009US	4622
959	7590	06/27/2006		EXAMINER
LAHIVE & COCKFIELD 28 STATE STREET BOSTON, MA 02109				LU, FRANK WEI MIN
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,873	RANGANATHAN, ANAND	
	Examiner Frank W. Lu	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 07 April 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-21 is/are pending in the application.
 - 4a) Of the above claim(s) 18-20 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-17 and 21 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 01 November 2002 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on April 3, 2006 has been entered. Since claims 22-48 have been canceled, the claims pending in this application are claims 1-21 wherein claims 18-20 have been withdrawn due to species election. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the response filed on April 3, 2006.

Sequence Rules Compliance

2. Sequencing listing filed on April 3, 2006 have complied with Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Drawings

3. The newly submitted Figures 6, 13, and 14 have been accepted by the office.

Specification

4. The disclosure is objected to because of the following informalities: (1) in line 1 of page 3 of applicant's remarks (amendments to the specification), "replace the paragraph beginning at page 25, lines 9-16" should be "replace the paragraph beginning at page 26, lines 9-16"; (2) in line 11 of page 3 of applicant's remarks (amendments to the specification), "replace the paragraph beginning at page 25, line 20, through page 27, lines 1-10" should be "replace the paragraph beginning at page 26, line 20, through page 28, lines 1-10"; and (3) in line 8 of page 5

of applicant's remarks (amendments to the specification), "replace the paragraph beginning at page 39, lines 1-20" should be "replace the paragraph beginning at page 40, lines 1-20".

Appropriate correction is required.

Claim Objections

5. Claim 12 is objected to because of the following informality: "the solid phase" should be "a solid phase".
6. Claims 7 and 15 are objected to because of the following informality: "the protein" should be "a protein".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
8. Scope of Enablement

Claims 1-3 and 5-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing the methods 1-3 and 5-8 using certain kind of DNA methylase when the DNA unit and the starting DNA construct are cleaved with an identical restriction enzyme, does not reasonably provide enablement for performing the methods 1-3 and 5-8 using any kind of DNA modification enzyme when the DNA unit and the starting DNA construct are cleaved with two compatible restriction enzymes wherein the two compatible

restriction enzymes are different restriction enzymes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that the methods 1-3 and 5-8 can be performed using any kind of DNA modification enzyme when the DNA unit and the starting DNA construct are cleaved with two compatible restriction enzymes wherein the two compatible restriction enzymes are different restriction enzymes. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the methods 1-3 and 5-8 can be performed using any kind of DNA modification enzyme when the DNA unit and the starting DNA construct are cleaved with two compatible restriction enzymes wherein the two compatible restriction enzymes are different restriction enzymes.

Claims 1-3 and 5-8 are directed to a method of assembling several DNA units in sequence in a DNA construct. First, according to step b) of claim 1, the starting DNA construct is cleaved with a restriction enzyme that is compatible with the restriction enzyme that cleaves the

desired DNA unit while according to step d) of claim 1, the ligated product formed by the desired DNA and the starting DNA construct is cleaved with a restriction enzyme that cleaves the desired DNA unit and a restriction enzyme that is compatible with the restriction enzyme. Since two compatible restriction enzymes can be considered as two compatible restriction enzymes that have different recognition sequences and can produce two compatible ends in two different nucleic acids wherein the compatible ends can ligate to produce a DNA construct, when the DNA unit and the starting DNA construct are cleaved with two compatible restriction enzymes (two different restriction enzymes), the ligated product formed by the desired DNA and the starting DNA construct do not contain the restriction sites of the restriction enzyme that cleaves the desired DNA unit or the restriction enzyme that is compatible with the restriction enzyme so that the ligated product formed by the desired DNA and the starting DNA construct cannot be cleaved with the restriction enzyme that cleaves the desired DNA unit or the restriction sites of a restriction enzyme that is compatible with the restriction enzyme as recited in step d) of claim 1. Second, according to step c) of claim 1, after treating the ligated product with a DNA modification enzyme, the restriction site at 3' end of the desired DNA unit is abolished. Since claim 1 does not limit that the DNA modification enzyme is a specific methylase and does not limit that the restriction enzyme or the compatible restriction enzyme is a specific restriction enzyme, and it is known that different methylases have different recognition sequences (see 2002-03 New England Biolabs Catalog, pages 95-99), different restriction sites on nucleic acids are blocked by different methylase and some restriction sites on nucleic acids cannot be blocked by methylases (see 2002-03 New England Biolabs Catalog, pages 17-19 and 64), it is unclear how the restriction site at 3' end of the desired DNA unit can be abolished after treating the

ligated product with any kind of DNA modification enzyme. Third, since there is no method step for cleaving the desired DNA unit, it is unclear how to inserting the desired DNA unit into the DNA construct as recited in step c) of claim 1.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether the methods 1-3 and 5-8 can be performed using any kind of DNA modification enzyme when the DNA unit and the starting DNA construct are cleaved with two compatible restriction enzymes wherein the two compatible restriction enzymes are different restriction enzymes.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-17 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 1 is rejected as vague and indefinite because it is unclear that a desired DNA unit in step c) of the claim is identical to one of DNA units in step a) or not. Furthermore, it is unclear whether each subsequent desired DNA unit in step e) has identical properties as each DNA unit in step a). Please clarify.

12. Claim 4 recites the limitation “the desired DNA unit” in step c) of the claim. There is insufficient antecedent basis for this limitation in the claim because steps a) and b) only have DNA unit and have no desired DNA unit. Please clarify.

Response to Arguments

In page 18, last paragraph of applicant's remarks, applicant argues that the amendments on claim 4 have overcome the rejection.

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because applicant does not amend “the desired DNA unit” in step c) of the claim.

13. Claim 8 recites the limitation “the DNA modification” of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase “DNA modification” in claims 1-3. Please clarify.

14. Claim 8 is rejected as vague and indefinite because it is unclear whether each subsequent desired DNA unit in step e) has identical properties as each DNA unit in step a) or not. Please clarify.

15. Claim 9 recites the limitation “said other desired DNA unit” in step b) of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase “other desired DNA unit” in step a) of the claim. Please clarify.

16. Claim 9 or 10 is rejected as vague and indefinite because it is unclear that the ligated product in step d) is the ligated product in step c) or a ligated product in step d). Furthermore, since claim 9 or 10 does not indicate that a subsequent desired DNA unit in step d) has identical properties as a desired DNA unit in step b), it is unclear whether the ligated product in step d) can be cleaved with said first restriction enzyme or not. Please clarify.

17. Claim 9 or 10 is rejected as vague and indefinite because it is unclear what each desired DNA in step e) represents for. Does each desired DNA in step e) represent for a desired DNA unit in step b) and a subsequent desired DNA unit in step d)? Please clarify.

Conclusion

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. No claim is allowed.

20. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.



June 20, 2006

**FRANK LU
PRIMARY EXAMINER**